BRITISH JOURNAL OF
TUBERCULOSIS
AND DISEASES OF THE CHEST

Vol. XLI. October, 1947 No. 4

GENERAL ARTICLES

SCAPULECTOMY AND THORACOPLASTY

By ALFRED J. COELLO
From Baguley Sanatorium.

One of the impressive things about thoracoplasty operations is the trauma involved, not only by the resection of many ribs but also by the extensive incision of the periscapular muscles. Attempts to minimise the trauma have been made by avoiding division of muscles (Finochietto) or by dividing those muscles along their less vascular line (Brock); and by reducing the amount of decostalisation by resecting the lower third of the scapula after the resection of the five or six upper ribs (Holman).

The importance of early obliteration of the extrapleural space for the prevention of infection in it is now well recognised. The obliteration of the extrapleural dead space left after thoracoplasty is not difficult from the front because the infraclavicular tissues easily retract. It can be helped by sandbags or binders. The real trouble is with the posterior and the postero-axillary walls, due to the presence of a rigid and uncollapsible bony wall—the scapula. Unless this bone is partially resected or falls in there will remain a relatively large dead space at the mercy of any infection of endogenous or exogenous origin.

It is easy to say that an extrapleural space infection should not occur. But its incidence is higher than commonly believed, and some estimates put it as high as 12 per cent. If it happens after a first stage further stages of the operation may be impossible, and, moreover a chronic discharging sinus through the wound may be left.

To prevent infection several technical modifications have been recommended. Thus, Ronald Edwards has obtained excellent results with a no-touch technique; Head recommended multiple and short incisions; Hart and Overholt the use of ultraviolet irradiation of the operating theatre; some surgeons use liquid penicillin at the end of the operation, and we have, since 1945, been using sulphathiozole-penicillin powder sprinkled over the operative area at the end of the operation with good results (*Tubercle*, December 1946). Nevertheless, I do not think the good results claimed for any particular method

can be attributed to it solely, however convincing the numbers. Individual technical skill is probably more important.

Although infection of the extrapleural space is often regarded as due to injury to lymphatic vessels or nodes found near the vertebræ, to necrosis of the intercostal structures, or to other endogenous sources, the simplest cause, contaminated air of the operating room acting on freshly traumatised tissues on an already weakened patient, is still a likely factor as pointed out by Overholt long ago. A first stage thoracoplasty is always a lengthy affair, and if it involves the division of the periscapular muscles, the resection of the four upper ribs and the mobilisation of the apex it hardly can be done in less than one hour and a half.

On the other hand, I believe that infection would not occur if the dead extrapleural space could be obliterated as soon as possible. I have not seen any case of extrapleural infection occurring after the scapula has fallen in, embedded into the extrapleural space left after decostalisation. Unfortunately this does not happen until the 7th and more often the 8th rib has been resected, requiring three stages or at least two extensive ones.

To spare the 6th and 7th ribs Holman advised resection of the lower third of the scapula. Unless there was marked paradoxical respiration, he believed that this could be done in one stage, provided that five ribs were resected in the required length. The usefulness of a partial scapulectomy to obliterate the extrapleural space was already acknowledged by Coryllos and Weinstein. Alexander also stated that resection of five or six ribs was sufficient if the lower third of the scapula is resected. He recommended the division of this bone following an oblique line that corresponds to the normal obliquity of the next adjacent intact rib, and even went as far as to say that the scapula can be resected as high up as its spine, at the level of the angle of the 4th rib.

All these authors, however, seem to have performed resection of the lower third of the scapula at the end of the operation as an alternative to further rib resection, conserving as much uninvolved lung and vital capacity as possible and eliminating pain and impaired movements of the shoulder due to impingement of the angle of the scapula on the intact 7th or 8th ribs.

Operative Technique

A partial scapulectomy with resection of practically half of the scapula can, however, be done prior to rib resection. It is easier then to retract the bone during the rest of the operation, and the degree of operative exposure obtained is much improved. Removal of part of the scapula also avoids the necessity of dividing the trapezius and rhomboid in their entirety, and of dividing any fibres of the latissimus dorsi. Only a few fibres of the trapezius and rhomboid need division along a short line parallel to the spinal border of the scapula. The skin incision can be the standard paravertebral incision, except that the distal flap should be undercut until the lower half of the scapula is sufficiently exposed.

The scapula is divided along an oblique line following the direction of the underlying 5th rib. This can easily be felt by introducing the hand through the triangular space formed by the rhomboid, latissimus and scapula.

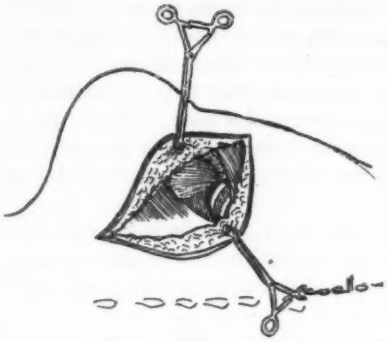

FIG. 1.

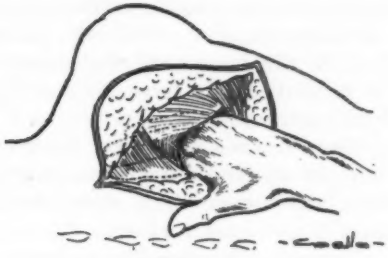

FIG. 2.

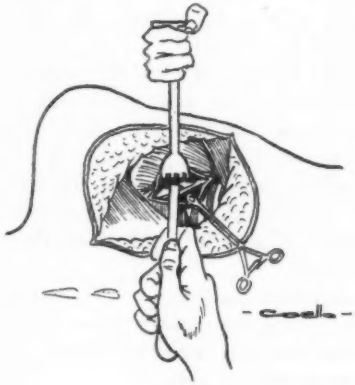

FIG. 3.

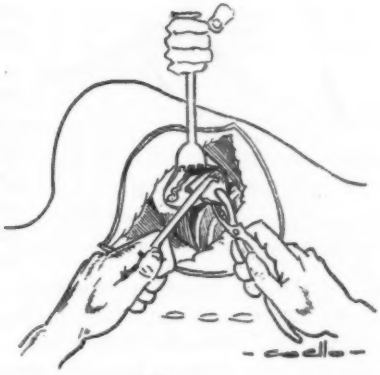

FIG. 4.

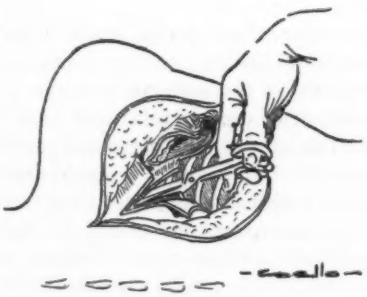

FIG. 5.

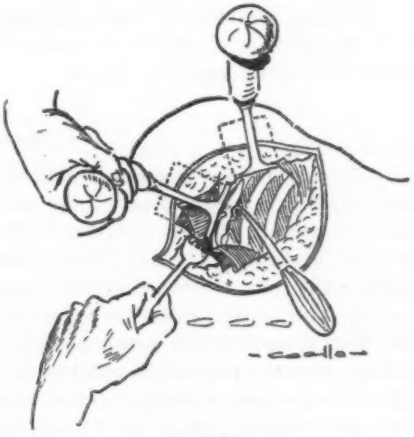

FIG. 6.

Once the line of the scapular division has been mentally drawn (it should be checked by moving the shoulder backwards and forwards to make sure that there will not be any impingement afterwards) a short incision is made along the spinal border of the scapula and both muscular flaps, infraspinatus and subscapularis, retracted. Tunnels are then made both behind and in front of the bone until they meet at the axillary border. The scapula can be divided with a large rongeur by successive bites or with a straight long bone cutter.

Once this has been done the free lower half of the scapula is gripped by a bone forceps and dragged out vigorously. It is freed from the infraspinatus, teres and subscapularis attachments easily by subperiosteal dissection with a raspatory or with scissors.

Immediately after this, in order not to waste time in picking up bleeding points, the pocket thus formed is tightly packed with swabs which are left in place until the end of the operation. By then bleeding should have ceased.

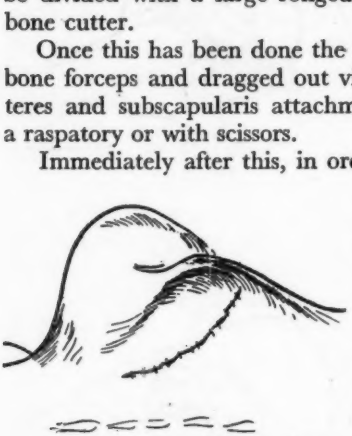

FIG. 7.

At this point division of a few fibres of the trapezius and rhomboid muscles should be sufficient to expose the 3rd rib. Resection of this rib may be difficult, but once it has been done subsequent resection of the 2nd and 1st ribs is easier than when other technique is used. This also applies to their anterior portions.

As the rib resection progresses operative exposure improves. This is due to the direction of retraction, for instead of separating the scapula towards the axilla, what remains of that bone can be lifted towards the shoulder by an assistant, the surgeon himself retracting the paravertebral side.

There is no need for any special instruments as with the Finochietto technique, although long instruments are helpful.

The only difficulty is when the patient is stout or heavily muscular, when it is advisable to divide the trapezius and rhomboid along the musculoplastic incision recommended by Brock.

Discussion

The advantages of doing a scapulectomy before rib resection, besides the ones already mentioned and those pointed out by Holman, are that it gives a better exposure of the operative field, particularly of the anterior portions of the 1st, 2nd and 3rd ribs; allows easier retraction of the scapula; and above all that the early obliteration of the extrapleural dead space is a great safeguard against subsequent infection. This is particularly important if an apicolysis has been done, for it is commonly after extensive mobilisations of the apex that a large amount of blood-stained fluid collects in that space and with it the risk of post-operative infection. The best prophylaxis against that infection is the early obliteration of the extrapleural space and this can be best achieved by early scapulectomy.

In cases of very localised apical lesions a one-stage thoracoplasty may suffice with removal of the three upper ribs completely plus enough length of the 4th and 5th ribs to allow the bedding in of the already half resected scapula. In one of our cases this bedding in of the scapula was actually obtained without resecting the 5th rib, but the scapula had been resected near its superior spine.

As I said before, not one single case of extrapleural space infection has occurred after early bedding in of the scapula.

It is difficult to obliterate that space by means of a partial scapulectomy once it is infected as suggested by Coryllos long ago even if a supplementary resection of the clavicle is done as recommended by Lambert. The infection is usually a mixed one, in reality a mixed extrapleural empyema, rather large, with multiple pockets and as a rule with a chronic discharging sinus that challenges any closing procedures at our disposal.

Conclusions

In order to prevent the development of an extrapleural space infection following thoracoplasty, the resection of half of the scapula is recommended. If this is done before the rib resection it has the advantages of giving a better operative exposure, makes the retraction of the scapula much easier and can spare most of the trapezius and rhomboid muscles. Also it makes it possible to do the operation in one single stage in cases of localised apical lesions provided that the scapula is resected near its transverse spine.

I wish to thank Dr. Trayer, Medical Superintendent, Mr. A. Graham Bryce, Consultant Thoracic Surgeon, and Dr. W. Anderson, Senior Medical Officer, for their help and great facilities afforded.

CHRONIC MILIARY TUBERCULOSIS

By WILLIAM N. ROGERS

From Epsom County Hospital.

Chronic miliary tuberculosis is now a well-recognised entity, mainly due to the work of Hoyle and Vaizey (1937). The following case well shows its bizarre symptoms and manifestations, and is recorded for their interest and because circumstances allowed unusually complete description.

The patient, a student nurse aged 20, was admitted to the sick bay of Epsom County Hospital on October 16, 1942, complaining of having felt giddy on waking up that morning. When she tried to stand her left leg was too weak to support her, she could not control the movements of her left arm and everything in the room appeared to rotate from right to left. On and off for about three years she had suffered from occipital headaches, and they had been rather severe for the previous three or four days. She never had nausea or vomiting.

She came from healthy country stock, but a maternal cousin was suffering from pulmonary tuberculosis. Her earlier history was irrelevant. She menstruated at the age of 13; the menses had always been irregular. In January 1941 she started nursing, having passed a medical examination at which a skiagram of the chest had been taken. Early in March 1942 she developed a

small abscess in the right index finger, which failed to heal after incision, leaving a discharging sinus until October, when after curetting healing occurred. On March 18, 1942, she lost the sight of the right eye suddenly, due to a large preretinal (sub-hyaloid) hæmorrhage. This condition improved slowly, and by July she was considered to have recovered. In August 1942 she accidently fell backwards and hurt her head, but was well again after a day's rest.

She was a well-nourished, intelligent girl. On admission her temperature was 103° F., her pulse rate 124, respirations 24, and blood pressure 160 mm. systolic, 110 mm. diastolic. Abnormal signs were present only in the nervous system. The left side of the face and the left arm and leg were paretic. Horizontal nystagmus was present, mainly on the left side, and her left abdominal reflexes were absent. Inco-ordination of movements was very prominent, especially in the left limbs, and was associated with intention tremor.

Ophthalmoscopic examination revealed a small scar and some blobs of pigment in the anterior part of the retina in the right eye. Difficulty in micturition for which she had to be catheterised, slight neck rigidity, pain along the spine, and difficulty in obtaining the left plantar reflex were present at some time during the next ten days, during which her condition improved on the whole, all the previous signs becoming less obvious. The temperature was remittent 98°-101°, and her blood pressure fell to 120/90. A lumbar puncture on admission revealed manometric pressure 130 mm.; cells 9 per c.mm. (lymphocytes 75 per cent.; polymorphonuclears 25 per cent.); proteins, 0·030 gm. per cent.; N.A., negative; Pandy, weakly positive; and a Lange test, sugar and chlorides all within normal limits. On October 19 the cells were 42 per c.mm. (polymorphonuclears 74 per cent.; lymphocytes 26 per cent.), and on November 6 6 per c.mm. (polymorphonuclears 16 per cent.; lymphocytes 84 per cent.), with proteins 0·150 gm. per cent., and Nonne Apelt and Pandy tests both positive. The fluids were sterile, and no organisms were seen in direct smear. Wassermann and Kahn reactions were repeatedly negative on cerebrospinal fluid and serum, and blood counts were within normal limits. The blood urea was 26 mgm. per cent. The urine contained a trace of albumen, pus cells and a few red cells, but no organisms. A skiagram of the skull was normal: no X-ray of the chest was taken. The possibility of tuberculous meningitis was considered, but was discounted because of her uninterrupted good progress. She was seen in consultation with a neurologist, and a provisional diagnosis of disseminated sclerosis was made. She was discharged from hospital on December 8, 1942, when only a slight and variable weakness remained in the left leg. In February 1943 she resumed her duties as a nurse at her own request.

Only a month later, however, she was readmitted to hospital, complaining of frequency and pain on micturition as well as hæmaturia of a week's duration. She was afebrile and in excellent condition. Harsh breath sounds were present in both interscapular areas. Her blood pressure 130 mm. systolic, 90 mm. diastolic. On palpation slight tenderness was detected in both loins. The left side of the face, the left arm, leg and foot were again paretic, but the reflexes were not materially affected. The choroid of the right eye showed

two new roundish white yellowish nodules about the size of a quarter of a disc, one at seven and the other at eleven o'clock. The area of pigmentation previously noted was still present. A small nodule was seen also at eleven o'clock in the left eye. The urine contained pus, red cells and tubercle bacilli, the latter proving to belong to the human strain on culture and animal inoculations. Skiagram of the chest revealed fine mottling in both lungs of the type characteristic of miliary tuberculosis. A descending pyelogram showed calcification in the upper pole of the right kidney and defects of filling in the upper and lower calyces. Cystoscopy revealed marked inflammatory changes, a granular appearance, hæmorrhages and ulceration in the mucosa of the bladder. Spasm prevented catheterisation of the ureters.

Course.—For the next five months her general condition was remarkably good with only slight loss of weight. Her temperature ranged from 97° to 99° F. up to May 1943, when it rose to 98°-102°, accompanied by a pulse rate of 64-100 and later 90-120; and respirations of 20-28. Pain after micturition increased gradually, and morphine had to be given eventually. The menses ceased. Slight dry cough was present, and some bronchial breathing and harsh breath sounds were found mainly in the right upper lung. The nodules in the right fundus appeared to be larger, more yellow, and with a surrounding pale area. The fundi were described by Dr. T. H. Whittington as being " albinotic and therefore the choroidal blood vessels can everywhere be seen through the retina. There are no acute or active signs in the eyes at present, and the white patches with fluffy edges and very little pigment are old ones of choroido-retinal atrophy. They are not miliary tubercle. On the other hand, they may be old areas of so-called tubercular disseminated choroiditis. They are not clear cut and show but little pigmentary disturbance, but the albinotic fundus may partly account for this " (Fig. 1). The radiological appearance of the chest showed typical miliary spread with tendency to confluence in the upper zones. In July 1943 she was transferred to St. Helier County Hospital, where she came under the care of Dr. H. F. Harewood, whom I wish to thank for having given me access to his notes. Weakness was present in the left side of the face, in the sternocleido-mastoid muscle, the left arm, leg and foot with loss of muscular tonus and tendency to foot drop. Rebound was detected in the left arm, and the reflexes in the left arm and leg appeared diminished as compared with the other side. The urinary symptoms were unchanged. The abdomen was tumid and tender, and a mild pyrexia persisted. The urine contained pus and tubercle bacilli. The blood urea was 35 mgm. per cent. Moderate hypochromic anæmia was present with a normal total and differential white count.

In October her condition deteriorated, and she was given a blood transfusion and a course of 20 grams of promanide in ten days. No change was noticed in her condition. Tubercle bacilli were never found in gastric residue or stools. In November a skiagram of the right sacro-iliac region showed early cystic changes. Her condition deteriorated rapidly, and eventually uræmic symptoms supervened. She died on February 6, 1944.

A necropsy was done the following day. The body showed marked wasting. The meninges were normal, the brain congested, and after fixation in formolsaline revealed symmetrical whitish friable, tumour-like masses about

2 cm. in diameter in the occipital areas of both hemispheres and a similar but smaller mass in the left lobe of the cerebellum. The pleural cavities were partially obliterated by adhesions. A caseous gland was found attached to the stem branch of the left lower bronchus, where it invaded the wall but apparently had not ruptured into the lumen. Both lungs showed the typical macroscopical appearances of miliary tuberculosis; no parenchymal lesion corresponding to the infected gland could be recognised. The heart and great vessels were normal. The peritoneal cavity contained a small amount of turbid fluid, and the peritoneum was grossly infiltrated by tubercles and fibrous exudate binding together the coils of small intestine. Numerous fleshy glands were present in the mesentry. Both kidneys were moderately enlarged and mainly consisted of pyelonephritic unilocular sacs. Ulcero-caseous changes and granulation tissue were prevalent, with small tubercles scattered through the remainders of the renal cortices. The ureters were thickened and shortened, the bladder small with thickened contracted walls and inflamed and ulcerated mucosa. The changes in the other organs, when present, were mainly histological. Microscopical examination showed in the occipital area of the brain a tuberculoma formed by smaller tubercles the centre of which was caseating. There was some small celled inflammation around the caseating area with a number of Langhans giant cells as well as definite formation of fibrosis, and in a few areas there was deposition of calcium. The appearance was that of a fairly long-standing process with probably some recent extension. In the cerebellum a tuberculous granuloma with a wall of fibrosis was found in the left lobe. There was no calcification. In the nearby cerebellar cortex there were numerous small areas of aspecific necrosis due to pressure of the tuberculoma on the blood vessels. I am indebted for the histological examination of the eye to the department of pathology of St. Thomas's Hospital. The report by Dr. Pirniger read: " At a place a little away from the posterior pole the choroid coat is thickened over a small area to about twice its normal width by a mass of recently formed fibrous tissue which is very lightly infiltrated by chronic inflammatory cells. No evidence of tuberculosis " (Fig. 2). A large number of typical miliary tubercles were seen in the lungs, in some areas aggregated. The larger proportion of these foci had a pale-staining acellular centre surrounded by a fibrous wall containing epithelioid cells and occasional giant cells. Others were much more cellular. The liver cells showed severe fatty and hyaline degeneration, there was generalised congestion of the organ, and at fairly frequent intervals miliary tubercles were found. The spleen showed congestion and increased hæmolysis. Disseminated in the parenchyma were numerous roundish foci formed by pale-staining tissue containing blood-vessels, some of which appeared to be newly formed fibroblasts. At the periphery were accumulated epithelioid cells, and both lymphocytes and giant cells were extremely scarce. Numerous miliary tubercles were seen in the cortex of the kidneys, usually containing a limited number of cells and showing a fibrous appearance. Towards the apex of the pyramids characteristic tuberculous tissue with widespread caseous necrosis nearly completely substituted the parenchyma. There was generalised vascular congestion and parenchymatous degeneration. The adrenals were mostly occupied by tuberculous masses. In the peritoneum were numerous fibrous tubercles.

FIG. 1.
Fundus of Right Eye. White patches and deposits of pigment in the choroid.

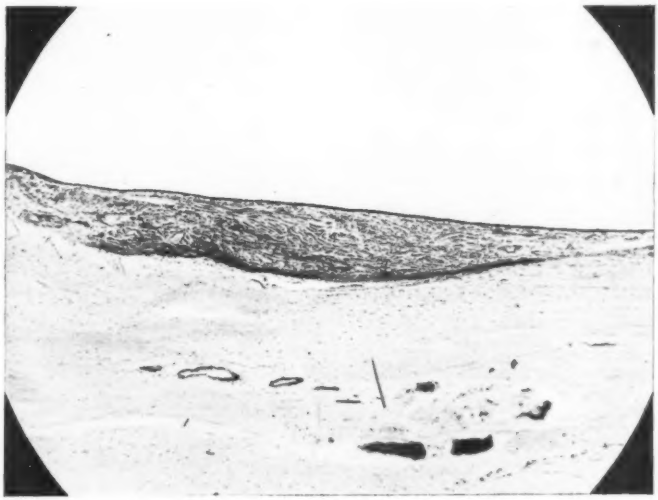

FIG. 2.
Section of Right Eye near the Posterior Pole. The choroid coat is thickened by young fibrous tissue infiltrated by chronic inflammatory cells. Hæmatoxylin and Eosin (x 35).

[*To face p* 82

Comment

In January 1941 this girl was medically examined, and a skiagram of the chest showed no abnormalities. In March 1942, whilst nursing, she developed an indolent abscess in a finger, progressing to a discharging sinus which lasted until October. It may be interesting to speculate on the ætiology of this process, but the available data are of no help. Her sudden blindness in March 1942, due to a preretinal subhyaloid hæmorrhage, may be considered an instance of Eales disease. Although the ætiology of this condition is far from established, its tuberculous nature has often been suggested and a close association with chronic miliary tuberculosis had been mentioned by Urbanek (1932). However, this association only occurred in three cases of Hoyle and Valzey's (1937) series.

In October 1942 she developed obscure neurological symptoms associated with pyrexia and changes in the cerebrospinal fluid. The pathological change found later in the brain and cerebellum was consistent with a belief that she was then suffering from tuberculosis of the central nervous system; and it is tempting to wonder if the occipital headaches of the previous three years were somehow connected with the same cause. She made on the whole a rapid and satisfactory recovery from this episode, and it is remarkable that, in view of her subsequent history, the disease henceforward should have remained quiescent in the central nervous system. Whilst the brain and especially the meninges are commonly affected in the terminal stages of chronic miliary tuberculosis, it is most unusual for neurological involvement to precede this form of disease. From December 1942 to March 1943 she appeared to be well, apart from some variable weakness mainly in the left leg. Eventually she was found to have renal tuberculosis and miliary tuberculosis in the lungs. On examining the eyes whitish patches were seen in the fundi, which had not been noted in October. These changes, which appeared to be due to areas of fibrous tissue infiltrated by chronic inflammatory cells, raise once again the uncertainties surrounding the problem of tuberculosis of the uveal tract. It is generally held that tuberculosis here is characterised by great pleomorphism and often fails to show anything specific either clinically or histologically. In Duke Elder's words, " the diagnosis of tubercle is greeted by the observer and his critics with enthusiasm or scepticism or violent disagreement according to their clinical bias." The same author says that " with the exception of acute miliary tuberculosis, ocular tuberculosis occurs with the greatest rarity in the presence of active tuberculosis elsewhere." In the present case a preretinal hæmorrhage was followed two years later by disseminated choroiditis at a time when she already had extensive tuberculous disease. Neither of these two ocular conditions have a well-defined ætiology, both are probably focal reactions which in this case must be attributed to tuberculosis. In Hoyle and Vaizey's series of cases choroidal tubercles are mentioned in two instances. Creveld and Huet (1943) record three cases of their own in children and one described by Ladenius in which chronic miliary tuberculosis was associated with changes in the fundi described as tubercles, healed tubercles or expired choro-iritis tuberculosa. In view of the diagnostic difficulties one may wonder if pathological examination would have confirmed these clinical views.

Death occurred in February 1944, eleven months after miliary tuberculosis had been recognised and twenty-three months after the first manifestation of a tuberculous disease. By this time very few tissues had escaped affection at one time or another.

This patient shows in an extreme form the varied, recurrent, dynamic evolution of the tuberculous disease. Repeated hæmatogenous disseminations of the disease seem to have occurred, no doubt with varying size of dose or even of virulence, and meeting a changing state of local and general immunity. The result was a clinical picture of unusual polymorphism.

Summary

The case is recorded of a young woman who suffered from a preretinal hæmorrhage followed a few months later by neurological symptoms which proved eventually to have been due to tuberculomas of the brain and cerebellum. After having made an apparent recovery for a year, she then developed renal tuberculosis and was found to have miliary tuberculosis of the lungs and disseminated choroiditis. Death occurred twenty-three months after the first ocular manifestations; by then tuberculosis had gradually affected most of the organs. The unusual features of this case and the varied picture of hæmatogenous tuberculosis are discussed.

REFERENCES

Creveld, S., and Huet, G. J. (1943): *Acta. Med. Scand.*, **113**, 135.
Duke Elder, W. S. (1940): "Text Book of Ophthalmology." Kimpton, London.
Hoyle, C., and Vaizey, M. (1937): "Chronic Miliary Tuberculosis." Oxford University Press, London.
Urbanek, J. (1932): *Trans. Ophthal. Soc. U.K.*, **52**, 227.

A CASE OF A LARGE THYMIC CYST SUCCESSFULLY REMOVED FROM THE ANTERIOR MEDIASTINUM

By JOSEPH SMART

From the London Chest Hospital.

Introduction

The occurrence of thymic tumours, although not common, is well recognised. The symptoms are few in the early stages, but later, pressure symptoms occur, owing to the increasing size and position of the tumour. Physical examination may reveal little, but radiologically a somewhat rectangular shadow is seen in the upper part of the anterior mediastinum, so that the whole of the mediastinum appears to be considerably widened in the postero-anterior view.

Generalised thymic enlargement is more commonly seen in infants or children, but when enlargement occurs in adults, malignant changes are usually present.

As is well known, the thymus may show generalised enlargement in myasthenia gravis, but a large benign cyst such as the one now described appears to be rare.

Case History

A female patient, aged 53, was first seen in September 1946. The history dated back one year, during which time she had a feeling of tightness in the neck which was more noticeable when lying down, but it was in no way disabling. A few months later this same peculiar feeling occurred if she were carrying anything heavy. Three months before being seen she had a little discomfort in the neck, with a slight, unproductive cough, which tended to be paroxysmal in character and was worse on lying down. For a short period before being seen she noticed a throbbing in the upper part of her chest, with some dyspnœa, again more marked when lying down. The general condition of the patient was extremely good. Her weight was steady and there was no hæmoptysis nor symptoms suggesting any parenchymatous lung lesion.

In the past history she had had a right mastectomy in 1936 for what was thought to be a carcinoma, but section showed this to be a chronic mastitis.

On examination she was a healthy-looking woman, afebrile, with a normal pulse and respiration rate. The veins of the neck were slightly distended when lying down, there was a slight, generalised enlargement of the thyroid gland, but no symptoms to suggest toxicity—*i.e.*, no tachycardia, no loss of weight, no exophthalmos and no sweating. The physical signs in the chest were as follows: on inspection, a scar from the right mastectomy was present, the movements were equal and full on both sides, the mediastinum was not displaced and the vocal vibrations were normal. On percussion the chest was resonant all over in front and behind, with the exception of slight impairment over the manubrium sterni, extending rather more to the right than to the left. The breath sounds were present and equal on both sides, they were vesicular in character, and there were no added sounds. The heart appeared to be a normal size and shape, the sounds were normal, the blood pressure being 120/80 and equal on both sides. There was no murmur to be heard over the impaired area.

The postero-anterior X-ray of the chest (Fig. 1) showed a large, rounded swelling in the upper part of the mediastinum, extending to the right and displacing the aorta to the left. Its outline was smooth and well defined, but its upper borders had a somewhat rectangular appearance. Apart from this the lung fields appeared to be clear and the diaphragms were in the normal position. Lung markings could be seen at the periphery of the tumour, although not in the central portion. The right base appeared to be clearer than the left, owing to the absence of the right breast. The right lateral X-ray (Fig. 2) showed the swelling to be situated in the anterior mediastinum, extending up to the clavicles and down to the fourth rib anteriorly. It was a homogeneous shadow and lung markings could be seen again. Slight osteo-arthritis of the spine, with ossification of the intervertebral ligaments, was also shown.

X-ray screening showed that the mass did not move on deglutition and appeared to pulsate, but it was thought that this was probably due to a trans-

mitted rather than a true pulsation, in view of the proximity of the mass to the aorta. The diaphragm moved well on both sides.

The patient was admitted to the London Chest Hospital on September 18, 1946. Her Wassermann reaction was negative, and a full blood count showed:

Red blood cells	4,900,000
Hæmoglobin	95 per cent.
White cells	6,400
Differential count:	
Polymorphs	69 per cent. = 4,416 per cm.
Lymphocytes	28 per cent. = 1,792 per cm.
Mononuclears	3 per cent. = 192 per cm.

The vital capacity was 1,750 c.c. and the blood cholesterol 180 mg. per cent.

A kymogram (Fig. 3) confirmed that the pulsation was transmitted.

A diagnostic artificial pneumothorax was then induced, and this showed that the tumour was completely separate from the lung tissue (Fig. 4).

The chest was explored on September 26, under Pentothal, gas, oxygen and cyclopropane anæsthesia. A postero-lateral incision was made, exposing the fifth rib, which was removed, and the pleural cavity opened. A large cyst, about the size of a cricket ball, which was extremely tense, was seen lying in the anterior mediastinum. It was partially mobilised, during which procedure it ruptured, the contents being a straw-coloured fluid. Following this, it was found to be impossible to free the cyst at its upper pole, as it was adherent to a firm mass of tissue and could not be removed through the chest. The lung was therefore re-expanded and the thoracic wall closed in layers. The patient was then placed in the supine position and a thyroid incision made in the neck. The supra-sternal space was entered by blunt dissection and the cyst, now collapsed, drawn up into the neck and removed, together with a small portion of firm material to which it was adherent. The cyst was quite free from the thyroid gland. The wound was closed in layers. The patient was given a blood transfusion throughout the operation, and her general condition was good.

During convalescence she developed a pyrexia with a swinging temperature between 99° and 101° for about three weeks, associated with a slight generalised rash. Radiologically the chest condition was satisfactory and only a small amount of fluid formed. This was explored on several occasions, and found to be a slightly blood-stained fluid, but with no pus cells or bacteria present. Her blood count, during this time, showed no increase in white cells; in fact, these were on the low side of normal, being 5,600. The differential count showed:

Polymorphs	71 per cent. = 3,976 per cm.
Lymphocytes	25 per cent. = 1,400 per cm.
Mononuclears	4 per cent. = 224 per cm.

The temperature gradually settled, and it was thought that the pyrexia was probably due either to a sulphonamide reaction, in support of which theory was the rash and low white blood count, or to the absorption of blood from the pleural cavity.

The patient was last seen on June 17, 1947. Her general condition was extremely good, the lung had completely re-expanded, and apart from slight

PLATE XII.

FIG. 1.

FIG. 2.

[*To face p.* 86

PLATE XIII.

FIG. 4.

FIG. 3.

tenderness in the wound she was very well. The present radiological appearances of the chest are normal.

The pathological report on the specimen removed showed that this was a cyst measuring 8 cm. by 5 cm. by 5 cm., which was attached by its upper pole to a firm mass. Section of the mass showed that this was thymic tissue, with typical Hassell's corpuscles in it. The section of the wall of the cyst showed that this was in actual fact multiple cysts, one of which was grossly distended, and the wall contained many other cysts which were flattened in it. The epithelium lining it was a single layer of flat epithelium which was not ciliated, and there was fibrous tissue present in the wall, together with collections of lymphatic cells. It was reported to be a thymic cyst.

Discussion

Mediastinal swellings of this nature are extremely difficult to diagnose, and the exact ætiology of this cyst remained unknown until the pathological section was available. Before operation, the differential diagnoses considered were, dermoid cyst, bronchogenic cyst, thyroid adenoma, aneurysm or possibly lipoma. The fact that the shadow did not show true pulsation and that the Wassermann reaction was negative made the possibility of an aneurysm unlikely, and in the postero-anterior X-ray the aorta appeared to be pushed across rather than dilated. The possibility of this being a thyroid adenoma was considered, especially as the patient had some thyroid enlargement; but against this, the tumour did not move on deglutition. In view of its size, however, it was felt that the absence of movement on deglutition did not entirely rule out a thyroid tumour. The position of the cyst in the anterior mediastinum raised the possibility of a dermoid cyst, but the uniformity of its structure caused doubt as to this diagnosis, as most dermoid cysts tend to have denser areas in one part or another of the tumour. Before operation it was thought that the most likely diagnosis was that of a bronchogenic cyst, a thyroid adenoma or possibly a lipoma. The fact that the cyst was completely free from the lung tissue does not exclude the possibility of a bronchogenic cyst.

Very little appears to have been written about cysts of the thymus. Ewing's " Neoplastic Diseases " (1940) mentions four types: (1) epithelial cysts occurring in the epithelial canals of the embryonal thymus, which may give rise to one or several cysts, these usually occurring in the horns of the glands. The present case may well be one of this type, as there were several cysts in the wall of the main cyst. (2) Dermoid cysts arising from the thymus, coming from the ventral extoderm or branchial clefts. Hare (1879) reported nine such cases. (3) Cysts caused by the invasion and distension of Hassell's corpuscles. Ribbert (1912) regarded these as derived from the persistent embryonal tubules. (4) Cystic lymphangiomas, occurring in the thymus. Seidel (1904) reported such a case in an infant of two years.

Fridjohn (1934) reported the post-mortem findings on an infant one day old, in whom a large thymic cyst was found, but the ætiology is not discussed. Speers (1938) reviewed the literature of thymic cysts and described a case of a thymic gland discovered at routine autopsy, where there was a history of

lead intoxication over a period of many years. Multiple cysts were present, two of which were larger than the rest, one measuring 8 mm. in diameter and the other 5 mm., the rest being minute. Their histological structure is discussed at considerable length, and it is concluded that the two larger ones probably owe their origin to persistent remnants of the thyro-pharyngeal ducts, while the minute ones are probably due to prolonged lead intoxication, resulting in lung sequestral cysts and cystic corpuscles. Kopac (1939) discussed thymic cysts in adults, and reviewed the literature. He described a thymus which resembled a bunch of grapes. It weighed 60 grammes, and the cystic mass was thought to be the left lobe, and the non-cystic mass associated with it the right lobe of the thymus. This was confirmed histologically. Syphilis could be ruled out entirely, and the author regarded the disturbance as due to areas of necrosis in the parenchyma of the thymus, owing to the degeneration of the thymic vessels. Hyde, Sellers and Owen (1944) reported a case of a thymic cyst occurring in the neck. As the thymus develops from the branchial clefts embryologically, this accounts for the position of this cyst.

Many other references to the thymus are to be found in the literature, but these refer largely to thymomas. Apart from Fridjohn's case, there appear to be no cases reported of large thymic cysts, with the exception of the dermoid cysts which may arise in the thymus. The exact ætiology of the present cyst is unknown.

The review of the literature shows that little is known about the ætiology of thymic cysts, and the two commoner views expressed are: (1) that the cysts develop as a result of arrest in fœtal development, due to congenital syphilis, and (2) that the cysts are due to a pathological process occurring in the parenchyma of the gland, which is otherwise normal.

REFERENCES

EWING, J., 1940, "Neoplastic Diseases," 1000, Saunders, Philadelphia.
FRIDJOHN, 1934, *Brit. Med. J.*, **2**, 553.
HARE, cited by Ewing.
HYDE, T. L., SELLERS, E. D., and OWEN, M., 1944, *Texas State J. Med.*, **39**, 539.
KOPAC, Z., 1939, *Beitr. path. Anat.*, **102**, 560.
RIBBERT, H., 1912, *Frankf. Z. Path.*, **11**, 209.
SEIDEL, Leipzig, 1904. Cited by Ewing.
SPEERS, F. D., 1938, *New York Med. Coll. and Flower Hosp. Bull.*, **1**, 142.

THE CLINICAL ASPECTS OF SARCOIDOSIS*

By CHARLES CAMERON

From the Department of Tuberculosis, the University of Edinburgh.

SARCOIDOSIS is a disease characterised by widespread tissue involvement and on account of its dissemination and the variety of tissues involved it is extremely difficult to give a defined description. While certain tissues may show major manifestations of involvement, others may be involved to a degree insufficient to

* A paper presented to the Sections on Dermatology and Disorders of the Chest at the International Conference of Physicians, held in London, September 1947.

produce clinical signs or symptoms, and regression of the lesions in one tissue and their development in another may make a changing and clinically confusing picture. I shall do no more than refer to the skin manifestations which have been described and discussed, and I shall confine myself to the more common signs and visceral manifestations. Even these may involve discussion on a regional rather than a general basis.

The disease has been described as a reticulo-endotheliosis and it may proclaim itself by a major manifestation in any of the tissues of that system. Other tissues may also be involved and the skin, the eye, mucous membrane of nose, pharynx, stomach, or intestinal tract, tonsils, salivary glands, lymph nodes, bones, liver, spleen, kidneys, heart, larynx, trachea, lungs may all be implicated, and lesions in the pituitary and male genital tract have been described. Not all of these tissues may be involved at one or at any time, and the cutaneous manifestations are inconstant.

It is extremely difficult to give any precise indication of the frequency of involvement of the different tissues, as workers in various branches of medicine see those cases which show involvement of organs in which they are interested. The dermatologist sees most of the cases with skin involvement, and the chest physician probably sees most of those in whom lung involvement of a sufficient degree to cause respiratory symptoms has taken place. In this way physicians may have different conceptions of the disease, and doubtless in the absence of skin or eye or gland involvement the diagnosis is frequently missed altogether or the patient with his changing picture may pass through many hands before a typical group of manifestations leads to a diagnosis.

Syndromes.—It is not surprising that where so many tissues are involved syndromes have been described. The best known of these are uveo-parotid fever (or Heerfordts' disease) and Mikulicz's syndrome. The ætiology of the latter is not settled. It may occur in conditions which are obviously not sarcoidosis or tuberculosis, but the complete syndrome may be merely an extension of the uveo-parotid condition. This condition has been very fully discussed by Garland and Thomson, who adduce strong evidence in favour of its tuberculous ætiology; but they state that the tuberculosis is of a peculiarly fibrosing and non-caseating type, and it is precisely on that point that the pathological diagnosis of sarcoidosis rests. Many of the recorded cases have had lesions in other areas of the body, including the myocardium, enlargement of peripheral glands and spleen, and radiographical changes in the lung roots and fields which are now generally accepted as being characteristic of sarcoidosis. The polyneuritis which sometimes accompanies the uveo-parotitis has, however, not been described in sarcoidosis, which does not involve the salivary glands.

Eye.—The eye changes in uveo-parotitis take the form of irido-cyclitis, sometimes with deposits in the iris leading to firm posterior synechiæ and often, but not invariably, to complete loss of vision. Exactly similar eye changes may occur in sarcoidosis with lesions in other parts of the body, but without involvement of salivary or lachrymal glands. Uveal involvement is in fact one of the common manifestations of sarcoidosis and probably occurs in half of the cases.

Skin.—The disease is intimately associated with the well-known skin lesions, but Boeck himself had stated in 1906 that the skin lesion is often associated with systemic manifestations. It is difficult to secure accurate figures of the incidence

of skin involvement. It is certainly frequent, but it may be absent in a considerable proportion of cases, just as involvement of other common sites of the disease may not take place. Its incidence has been placed at 40 per cent.

Bone.—The bone changes originally described by Jungling under the title of osteitis tuberculosa multiplex cystica occur in a varying percentage of cases, probably not exceeding 20 per cent. The typical cyst-like form which is so easily demonstrated radiographically in the heads of the phalanges, metacarpals, and metatarsals gives a useful confirmation of the diagnosis, but its restricted incidence should be remembered and also the fact that this is not the only form of bone change which the disease can produce. The bone marrow may be involved in a diffuse granulomatous process which may produce no radiographical changes or may give rise to a diffuse reticulated rarefaction of the bone shaft. This type may cause broadening of the bone shaft, and sometimes destruction and deformity of the digits. Other bones than the distal extremity bones may be involved and changes may be found in the long bones of the extremities. Fusiform swelling of the fingers and toes may accompany the bone involvement. It should be remembered that bone lesions may recede like lesions elsewhere and may only be radiographically evident at a certain phase of the infection.

Lymph Glands.—The lymph glands are frequently enlarged. This enlargement is present at some time or other in probably 90 per cent. of cases, and in a further percentage there is glandular involvement, but not of a sufficient extent to be clinically recognisable. The latter group probably represents disease in a regressive phase. Schaumann has pointed out th frequency of tonsillar involvement even when the tonsils appear to be healthy.

Liver and Spleen.—The liver and spleen are frequently involved. Enlargement is rarely gross, but that occasionally happens with the spleen.

Lungs.—Sarcoidosis is in no sense a respiratory disease, but the lungs are involved in the process in a majority of cases and the degree of involvement often bears little relation to the symptomatology. Symptoms may be absent, or may be no more than slight cough and dyspnœa. In progressive cases dyspnœa may be severe and is then related to the fibrosis and emphysema which are the end-result of the pathological process. Physical signs may be scanty or absent. When present, they are those of the fibrosis and emphysema and are in no way specific. If the disease assumes a caseating type and ulcerative tuberculosis develops, the signs are the manifold signs of that condition.

The sarcoid changes develop in the interstitial tissues of the lung and follow the track of the perivascular and peribronchial lymphatics. They are most marked in the interlobular septa and in the subpleural layers, and are often most dense around the hila. The glands in the hilar regions are often enlarged. The presence of lung involvement may be a chance radiographical finding and radiography of the chest should never be omitted when sarcoidosis is suspected. In a strict sense the disease can only be diagnosed by histological examination of involved tissue, and diagnosis, apart from that, is presumptive. Most radiographical diagnosis is up to a point presumptive, but the radiographical appearances of the sarcoid lung do often follow a pattern which is suggestive of the condition. Sometimes the relationship of the lung changes to sarcoidosis can only be presumed from the presence of the disease elsewhere.

The pathological basis of the disease is the epithelioid tubercle, and in the active stage of the disease dissemination of these tubercles often gives a finely nodular radiographical picture which may resemble closely blood-borne forms of tuberculosis. These disseminations may be widespread and bilateral, and are usually most dense in the central and lower zones, but they may be localised to areas of the lungs. Often coarser nodules are present, and they too may be diffusely distributed or localised. This purely nodular type is uncommon, for in addition to the tubercles there are always accompanying hyperplastic changes in the peribronchial and perivascular lymphatics, and even in blood-vessels, which make the picture a composite one, consisting of nodules and irregular, ill-defined strands which give a reticular background to the picture. It is this composite type of X-ray picture which is suggestive of sarcoidosis, but occasionally the picture is confused by dense conglomerate shadows which are difficult to place in any pathological category. Hilar and mediastinal gland masses are seen in a majority of cases. They may be the sole radiographical finding or they may accompany, or precede, or follow the changes in the lung fields. The hilar enlargement is invariably bilateral and occasionally gross. Lobar or segmental lung collapse caused by the glands and pleural effusion occasionally occur. The possibility of sarcoidosis should always be kept in mind when confusing lung X-ray appearances are encountered, especially where there is obvious enlargement of lung root and mediastinal glands. The one thing common to these X-ray changes is their preponderance over clinical symptoms, and that fact alone is suggestive of the diagnosis. The different pictures may represent stages of the disease and all may be, up to a point, reversible. Occasionally, especially in the nodular types, practically complete clearing may take place. Progressive cases may advance to extensive fibrosis and emphysema, but this is unusual. Some of this latter type have been observed to develop lung cavities without tubercle bacilli in the sputum.

Other Areas.—Less usual sites of sarcoid involvement are the pituitary, mucous membrane of nose, trachea, stomach and bowel, and the heart, muscle and kidneys. Hyperglobulinæmia with a reversal of the albumin-globulin ratio is common but not specific. Eosinophilia occurs in a percentage of cases, and monocytosis may develop during phases of disease activity.

Diagnosis.—Sarcoidosis thus cannot be looked upon as a disease of one organ or system. It is essentially a generalised infection whose local manifestations may bring the patient to physicians whose interest lies in different fields of medicine. Probably a minority of the cases have skin manifestations. Diagnosis opens a wide field of possibilities and can often only be settled by biopsy of affected material. If the lung appearances are taken alone such varying states as miliary tuberculosis, carcinomatosis, pneumoconiosis, chronic passive congestion, leukæmia, the reticuloses, and fungus infections must be taken into account. Often the combination of evidence of disease, past or present, of more than one structure or organ with the X-ray changes in the lungs, and possibly in bones, may warrant a presumptive diagnosis. In this connection one should remember that the clinical picture may never develop to classical completeness, and that final proof of the diagnosis may be impossible.

Tuberculin Sensitivity.—The tuberculin test in uncomplicated sarcoidosis is usually negative, but often reactions to high strengths of tuberculin are obtained. The presence of a positive reaction need not invalidate the diagnosis.

Ages.—The majority of cases occur between the ages of twenty and thirty, but cases have been described in childhood and infancy. The disease is characterised by chronicity and it may be difficult to determine the age of actual onset.

Prognosis.—It is this element of chronicity which makes prognosis so difficult. Some cases develop caseating tuberculosis, and if we accept the identity of the two conditions the possibility of that must be envisaged. At the other extreme are cases which regress and make an apparently complete recovery. An intermediate group remains stationery after degrees of organ damage, such as loss of vision or extensive lung fibrosis, have taken place. Progression of disease in lungs, myocardium, or kidneys may lead to a fatal issue without caseating tuberculosis developing. When Schaumann employed the term lymphogranulomatosis benigna he did so to differentiate the condition from Hodgkin's disease, and he pointed out that the course of the condition might be other than benign. The course of the disease is always long and it is rarely possible to prognosticate regarding its issue.

OBSERVATIONS ON SARCOIDOSIS*

By CLIFFORD HOYLE

From King's College Hospital and Brompton Hospital.

Introduction

It is now exactly seventy years since Jonathan Hutchinson (1877) described lupus pernio. Of the many inquiries into sarcoidosis since that first account, those of Boeck and Schaumann, and those of our distinguished guest Professor Pautrier, have been outstanding for their excellence. Yet for several reasons sarcoidosis is still difficult to define. The clinical features taken alone are often deceptive, even when conforming to accepted patterns. Neither a negative tuberculin reaction nor the positive skin changes produced by antigens from sarcoid tissue (Williams and Nickerson, 1935; Kveim, 1941; Danbolt, 1943; Putkonen, 1943) are reliable for diagnosis (Carnes, 1947). The serum globulin is not invariably raised, nor is an increase by any means confined to sarcoidosis (Bing, J., 1940). The usual sources of biopsy tissue are often denied, and newer ones, the tonsil and bone marrow, are either less reliable or, like the liver, less readily available as they involve a skilled technique. Even with such resources and with every test at hand, the recognition of sarcoidosis as a separate morbid entity is still a contentious issue. It is not surprising therefore that diagnostic standards vary greatly, so much so that many accounts in the literature leave a doubt of their authenticity.

* A paper presented to the Sections on Dermatology and Disorders of the Chest at the International Conference of Physicians, held in London, September 1947.

Clinical Material

My own experience of sarcoidosis is small, for among 135 patients whose clinical and other features gave some reasons for considering it, the diagnosis could be regarded as endorsed in 16 only, by histological support in each case. Another 14, though probable examples, were unconfirmed; and in 32 others alternative diagnoses seemed just as likely. Of the remaining 73 patients, 53 had chronic miliary tuberculosis, verified by necropsy in 14, and in the others by finding bacilli eventually, or caseous lesions in glands, skin, or other organs. Three others had atypical Hodgkin's disease, 2 lymphoblastic leukæmia, 4 carcinomatosis, 2 the so-called adenomatosis of the lungs, 3 pulmonary congestion from mitral stenosis, and 6 a chronic respiratory infection with bronchiolitis the probable explanation. I have excluded dust diseases and chronic pneumonias from this series, for although they may resemble pulmonary sarcoidosis in some respects, they are not often mistaken for it.

Pulmonary Forms

The comparative incidence of the various features of sarcoidosis is still debated, mainly because short series fail to picture the whole disease (Schaumann, 1934; Longcope and Pierson, 1937; Hantschmann, 1939; and Reisner, 1944). In sequence, if not at the start, the lesions are apt to be widespread. Massive spleens or livers have been infrequent in my own cases, and only once have bones been thought to be affected. Nor has evidence of myocardial damage been found, though Longcope (1941) and Rich (1946) both drew attention to its occasional importance.

In contrast the lungs are among the organs most commonly affected. The characteristic form of the disease is a combination of lymph gland enlargement, skin lesions, and uveo-parotitis. In this triad the intra-thoracic lymphatic system takes a prominent share, for enlargement of the broncho-pulmonary and mediastinal lymph glands is an early and persistent feature (Fig. 1). Usually the glandular shadows are symmetrical and large, and they are well defined until the lungs become involved.

Here the changes begin either with a reticulated or with a miliary mottling. Reticulation is seen at first radiating from the glands (Figs. 2 and 2a). It extends in time towards the periphery as a latticed pattern becoming gradually finer and looking like a net spreading over the lung fields. Sometimes it is the most marked feature, though I have never seen it appearing unless some glandular enlargement was already present. When reticulation is pronounced and when it has been present for some time it becomes much denser and coarser, obscuring the lung fields, especially near the roots and below that level (Figs. 3 and 4).

The miliary type of sarcoidosis shows nothing distinctive of its origin (Fig. 5). In size, in distribution, in density and in numbers, the shadows conform to the picture of miliary tuberculosis, with the same variations. Focal shadows form a third radiological type of the disease. They are coarsely nodular, coalescent and sometimes large. Both miliary and focal varieties may eventually resemble diffuse fibrotic tuberculosis when the lesions have contracted and scarred.

These various changes are not often marked by important symptoms or signs. Indeed, the disparity between the fitness of the patient and the anatomical severity of the disease is very striking. It can be matched only by a few other active disorders which affect the lungs so widely, and, at the same time, show a comparable silhouette—by some dust affections, by chronic miliary forms of tuberculosis, by the lipoid diseases, and by a few other still greater rarities. Minor degrees of breathlessness and a dry cough are not unusual; anything more is deferred until late in progressing forms of the disease. Breathlessness may then become extreme, for at this stage there is always a diffuse fibrosis of the lungs with severe structural damage to alveoli. The clinical course and the distribution of the morbid changes along the peribronchial and perivascular lymphatics (Fig. 6) are like those which Schürmann and others found with lymphogenous chronic miliary tuberculosis. At this stage pulmonary heart disease is added to the picture, though it takes years for this sequence to mature. When it does, right heart failure is not long delayed, and is soon fatal. Two of my patients died respectively eleven and fifteen years after recognition, within a few years of the first appearance of troublesome shortness of breath, and within a month or two of the onset of œdema (see Fig. 13).

Perhaps of all sarcoids of the lungs the miliary form most nearly defies distinction. There is the same benign symptomatology and scarcity of signs as with some examples of chronic miliary tuberculosis (Fig. 7), the same indolent course, the same association with similar extra-pulmonary lesions, the same radiological appearance and the same fibrosing epithelioid structure of the lesions. One might add that with the tuberculous cases there is often the same difficulty in tracking down the causal organism, as the many suspected but unproven cases show. Many of my series were found to be tuberculous only long after discovery (Figs. 8, 9 and 10), and it seems likely that more complete surveys will reduce the proportion of doubtful examples where sarcoidosis can otherwise be considered an alternative diagnosis.

Pulmonary sarcoidosis is well known to be followed by phthisis, and both the frequency and the significance of the complication are uncertain. Pinner (1938) and Rubin and Pinner (1944) traced 44 recorded necropsies on sarcoid patients up to three years ago: 14 showed pulmonary tuberculosis. Reisner (1944) has since reported 7 deaths in a series of 35: 3 died from chronic pulmonary tuberculosis and 2 others had disseminated tuberculosis at necropsy. Hagn-Meincke (1944) had 3 with pulmonary tuberculosis, 1 other with a tuberculous abscess, and 2 deaths in others from tuberculous meningitis in his series of 26. Two of my patients eventually developed fibro-caseous tuberculosis with cavities (Figs. 11, 12 and 13). The tuberculous disease was mainly in the upper lobes (Fig. 14) and was related marginally to hyalinised and epithelioid sarcoid tissue (Fig. 15) in a way that pointed to one morbid change succeeding the other in spreading sequence through the lungs. Both patients developed clinical phthisis with a positive sputum some months before they died, the organisms from one being of the human type. Both of them also showed reciprocal remission of cutaneous lesions, as in lupus, when their clinical tuberculosis began. Several writers (Schaumann, 1922 and 1936; Goldschmidt, 1925; Bonnevie and With, 1937) have described how resistant

cutaneous sarcoids resolve for the first time in a protracted course along with the appearance of cavitary phthisis, with tubercle bacilli in the sputum and with Mantoux conversion—a change quite unaccounted for.

These progressive pulmonary forms of the disease are, however, exceptional. Both massive and miliary lesions often remain unchanged for long periods or resolve slowly, after surprisingly little harm to the patient. If there is nothing more than glandular enlargement and reticulation a return to normal is even commoner. Such complete resolution is surprising if these reticulations are always due to granulomatous foci. Also, where they disappear eventually, they seem to persist for about two years (Figs. 16, 16a, 17 and 17a), receding only after the hilar glands. It looks as though the reticulation may sometimes be due to mechanical causes, blocked lymphatic drainage from the lungs accounting for some of the reversible changes. Comparable reticulations which disappear leaving normal lung fields are also seen when tuberculous adenitis affects the broncho-pulmonary glands massively and symmetrically.

Tuberculin Sensitivity

Patients with sarcoidosis are often insensitive to tuberculin, but when they are we do not know whether they were sensitive or not before acquiring the disease. Figures for the incidence of a negative Mantoux reaction in patients with the disease compared with the population incidence for their age groups are unconvincing that the disease is capable of causing loss of a previously acquired sensitivity. At any rate, when sarcoidosis develops after known clinical tuberculosis the sensitivity usually remains. An instance of this in my own series was a patient who had cutaneous sarcoidosis of the right shoulder with the usual histology. This woman had arrested fibro-calcified tuberculosis of both lungs for which she had been under treatment some years before, when she had a cavity and a positive sputum. In spite of the sarcoid she still has a strongly positive Mantoux reaction. Cameron and Dawson (1946) recently recorded a similar finding, where torpid pulmonary tuberculosis was succeeded by uveitis, an accompanying adenitis and skin lesions showing the histological picture of sarcoidosis. Moreover, when sarcoidosis is followed by progressive tuberculosis, skin sensitivity increases or returns (Funk, 1935; Schaumann, 1934; Warfvinge, 1943; and Reisner, 1944).

The argument that tuberculin insensitivity separates sarcoidosis from tuberculosis is a dangerous one, for those very examples of chronic tuberculosis which most closely resemble sarcoidosis sometimes have a negative Mantoux reaction (Hoyle and Vaizey, 1937). Brooks and his colleagues (1940) found this true also for iridocyclitis. Moreover, some tuberculous animals fail to develop tuberculin sensitivity—the rat, for instance. One patient who came under my observation illustrated the difficulties well. She was a young woman who had a trivial hæmoptysis from small apical infiltrations (Fig. 18) which eventually healed. Two years after this initial symptom she developed cervical adenitis, a gland from which showed tuberculous change with caseation. But the most striking feature at this time was enlargement of the hilar glands (Fig. 19), followed by reticulation and scattered shadows in both lung fields. They reached proportions which quite belied the fact that she remained symptomless and fit. After about two years the hilar glands receded (Fig. 20), and

after that the lung fields cleared rapidly, leaving a normal picture, except for the calcified apical disease (Fig. 21). Now throughout the whole of this ailment she retained a negative Mantoux reaction, even up to 1 in 10. It only became positive eight years after the original hæmoptysis, following a confinement, and without any other demonstrable change. Although bacilli were never found, the separate features of her illness are linked together as parts of the same tuberculous process by the glandular histology. But the main changes in the lungs radiologically, the persistently negative Mantoux reaction, and the benign course are all features of a sarcoid-like condition. The pathological counterpart was described by Mylius and Schürmann (1929), who found sarcoid and caseating lesions side by side in the lungs of a patient whose skin reactions to both human and bovine tuberculin were negative in life; and they failed to demonstrate bacilli even by animal inoculations.

All these observations suggest two reflections: that patients with sarcoidosis and a negative Mantoux may not previously have had a positive reaction; and that the disease could still be tuberculous in spite of a persistently negative reaction, belonging then to a deceptive class where tuberculin sensitivity does not develop or is readily suppressed.

Relationship to Tuberculosis

The evidence of a causal relationship between tuberculosis and sarcoidosis was thoroughly reviewed by Pinner in 1938. Direct evidence has reached a deadlock because tubercle bacilli have so rarely been found in sarcoid lesions or been transmitted from them to animals (Boeck, 1905; Wende, 1911; Ruete, 1922-23; Goeckerman, 1928; Dittrich, 1931; Pautrier and Glasser, 1936). Kissmeyer (1932), Snapper (1938), Longcope (1941), Rich (1946), and many others have failed with such attempts; nor have any of my own cases given positive results. Whether these failures outweigh the few successes is a matter of opinion. The situation is not unique, for we are familiar with the difficulty of finding causal organisms in very indolent infections—a difficulty sometimes shown by tuberculosis. If sarcoidosis is in fact tuberculous, then the organisms must have a very limited viability in affected tissues. In conformity Kyrle (1921 and 1927) found acid-fast organisms in recent cutaneous sarcoids, whereas they were absent from the same lesions a few weeks later; and Pinner (1945) had the same experience with lymph glands from a patient who had benign tuberculosis of many organs successively. Glands removed at a fortnight's interval both showed epithelioid-celled tubercles and little caseation, with human tubercle bacilli on the first occasion, but none on the second, even by culture and animal inoculation.

Further evidence bearing on the problem was recently produced by Warfvinge (1943). A young woman suffering from uveo-parotitis and adenitis was thought to have sarcoidosis on examination of tissue from a parotid gland and a lymph node. Later she developed extensive pulmonary tuberculosis with virulent human tubercle bacilli in her sputum. Inoculation of these living organisms into her own skin led to the formation of a nodule showing sarcoid changes, but no necrosis and no detectable tubercle bacilli. It is open to regard her illness as tuberculous throughout, or as due to sarcoidosis followed by tuberculosis independently. If we accept the former, then the validity of

the histological distinction between the two conditions has to go; and if the latter, then sarcoid lesions can clearly be produced by living virulent tubercle bacilli in the human subject already affected by the disease.

Although I hesitate to intrude upon the morbid histology, I feel that there is room for criticism of some expert views. The separation of sarcoidosis from tuberculosis on histological grounds would be more convincing if it had been shown that tuberculosis was incapable of producing lesions with a sarcoid pattern. On the contrary, comparative pathology provides numerous examples to start with. Cobbett, L. (1907 and 1917), Gloyne and Page (1923), Jadassohn (1934), and Wessels (1941) all found that tuberculosis in the rat remains epithelioid-celled and rarely shows necrosis or caseation. Avian tuberculosis in mice (Gunn, Nungester and Hougen, 1934) and swine (Feldman, 1938) is similar. There is a variety of tuberculosis in the horse (Nocard, 1895; and Nieberle, 1931 and 1932) with tough massive lesions in the lungs, spleen, liver and lymphatic glands, no tendency to caseation or calcification, and few bacilli. Dogs (Feldman, 1931) and cats (Griffith, 1911) may show the same kind of productive change; and in rabbits rapid destruction of tubercle bacilli is associated with a predominantly epithelioid-cell reaction (Lurie, 1932). These variations can also occur in man. Many years ago Ziegler (1906) described "large cell hyperplasia" as a phase of tuberculous lesions where caseation was exceptional. It occurs not only in hyperplastic tuberculosis of lymph glands and synovial membranes, but also in regional lymph nodes draining tuberculous tissues, as Clegg has recently shown once again. Lemming (1940 and 1942) produced sarcoid skin lesions and regional adenitis with inoculations of B.C.G. into patients with sarcoidosis. All these examples reveal the same recognition of more than one histological design. Their importance for the interpretation of sarcoidosis is that their prescriptive characteristics are the same. They are, in fact, "sarcoid" lesions produced by the tubercle bacillus.

The excuse of the clinician for discussing problems of ætiology in sarcoidosis is that they are his practical concern. However we view the disease—whether from its clinical appearance and course, its radiology, its morbid histology, or its intractability to transmission—the similarity to known examples of tuberculosis is a constantly recurring feature. Although this similarity is no proof of identity, it is so close that separation has become meaningless. In successive phases the problems of sarcoidosis have been regarded largely as the restricted problems of an uncommon disorder. The link with tuberculosis compels a truer perspective by which they are seen to bear directly upon some of the most obscure problems of this major disease.

I am indebted to many colleagues for allowing me to see their patients and for generously permitting the use of records; in particular to Dr. Maurice Davidson, Dr. Sydney Thomson, Dr. J. L. Livingstone, Dr. Archibald Gilpin and Dr. J. G. Scadding. Dr. J. W. Clegg kindly placed all his skill and necropsy material at my disposal, and Dr. Jean Simpson did much of the recent clinical follow-up of my patients.

REFERENCES

Bing, J. (1940): *Acta Med. Scand.*, **103**, 547.
Boeck, C. (1905): *Arch. Dermat.*, **73**, 71.
Bonnevie, P., and With, T. (1937): *Arch. f. Dermat.*, **175**, 407.

BROOKS, W. D. W., JULER, F. A., and WILLIAMS, E. R. (1940): *Brit. J. Ophthal.*, **24**, 317.
CAMERON, C., and DAWSON, E. K. (1946): *Edin. Med. J.*, **53**, 465.
CARNES, W. H. (1947): Personal Communication.
COBBETT, L. (1907): "Second Interim Report of the Royal Commission on Tuberculosis." Part II, Appendix, Vol. II, 1190. H.M. Stat. Office, London; and (1917), "The Causes of Tuberculosis." Cambridge University Press.
DANBOLT, N. (1943): *Acta Med. Scand.*, **114**, 143.
DITTRICH, O. (1931): *Dermat. Z.*, **60**, 395.
FELDMAN, W. H. (1931): *Amer. J. Path.*, **7**, 147.
FELDMAN, W. H. (1938): "Avian Tuberculosis Infections." Baillière, Tindall and Cox, London.
FUNK, C. F. (1935): *Arch. f. Dermat.*, **167**, 560.
GLOYNE, S. R., and PAGE, D. S. (1923): *J. Path. and Bact.*, **26**, 224.
GOECKERMAN, W. H. (1928): *Arch. Dermat.*, **18**, 237.
GOLDSCHMIDT, W. N. (1925): *Arch. f. Dermat.*, **149**, 331.
GRIFFITH, F. (1911): "Final Report of the Royal Commission on Tuberculosis," Part II, Appendix 5, 203. H.M. Stat. Office, London.
GUNN, F. D., NUNGESTER, W. J., and HOUGEN, E. T. (1934): *Proc. Soc. Exp. Biol. and Med.*, **31**, 527.
HAGN-MEINCKE, F. (1944): *Acta Tubercul. Scand.*, **18**, 1.
HANTSCHMANN, L. (1939): *Ergebn. f. ges. Tuberkulosefor.*, **9**, 1.
HOYLE, C., and VAIZEY, M. (1937): "Chronic Miliary Tuberculosis." Oxford Univ. Press, London.
HUTCHINSON, J. (1877): "Illustrations of Clinical Surgery," i, 39. Churchill, London.
JADASSOHN, W. (1934): *Bull. Soc. Franç. Dermat.*, **41**, 1344.
KISSMEYER, A. (1932): "La maladie de Boeck: Sarcoides cutanées bénignes multiples." Masson, Paris.
KVEIM, A. (1941): *Nord. Med. Tidskr.*, **9**, 169.
KYRLE, J. (1921): *Arch. f. Dermat.*, **131**, 33.
KYRLE, J. (1927): "Vorlesungen über Histo-Biologie der menschlichen Haut und ihrer Erkrankungen," **2**, 207. Springer, Berlin.
LEITNER, ST. J. (1942): "Der Morbus Besnier-Boeck-Schaumann." Schwabe, Basle.
LEMMING, R. (1937): *Nord. Med. Tidskr.*, **14**, 1822.
LEMMING, R. (1940): *Acta Med. Scand.*, **103**, 400.
LEMMING, R. (1942): *Acta Med. Scand.*, **110**, 151.
LONGCOPE, W. T., and PIERSON, J. M. (1937): *Bull. Johns Hopkins Hosp.*, **60**, 223.
LONGCOPE, W. T. (1941): *J. Amer. Med. Assoc.*, **117**, 1321.
LURIE, M. B. (1932): *J. Exp. Med.*, **55**, 31.
MYLIUS, K., and SCHÜRMANN, P. (1929): *Beitr. z. Klin. d. Tuberk.*, **73**, 166.
NIEBERLE, K. (1931): *Ergebn. d. allg. Pathol.*, **25**, 63.
NIEBERLE, K. (1932): *Ibid.*, **26**, 711.
NOCARD, E. (1895): "The Animal Tuberculoses, and their Relation to Human Tuberculosis." Trans. by Scurfield. Baillière, Tindall and Cox, London.
PAUTRIER, L. M. (1936): *Bull. Soc. Franç. Dermat.*, **43**, 505.
PAUTRIER, L. M., and GLASSER, R. (1936): *Bull. Soc. Franç. Dermat.*, **43**, 505.
PINNER, M. (1938): *Amer. Rev. Tub.*, **37**, 690.
PINNER, M. (1945): "Pulmonary Tuberculosis in the Adult." Thomas, Springfield.
PUTKONEN, T. (1943): *Acta Derm. Vener.*, **23**, Supp. 10.
REISNER, D. (1944): *Amer. Rev. Tub.*, **59**, 289 and 437.
RICH, A. R. (1946): "The Pathogenesis of Tuberculosis." Thomas, Springfield.
RUBIN, E. H., and PINNER, M. (1944): *Amer. Rev. Tub.*, **49**, 146.
RUETE, A. (1922): *Dermat. Z.*, **37**, 129.
SCHAUMANN, J. (1922): *Acta Derm. Ven.*, **3**, 679.
SCHAUMANN, J. (1934): *Bull. Soc. Franç. Dermat.*, **41**, 1296.
SCHAUMANN, J. (1936): *Brit. J. Dermat.*, **48**, 399.
SNAPPER, I. (1938): "Pseudo-Tuberculosis in Man." Bohn, Haarlem.
WARFVINGE, L. E. (1943): *Acta Med. Scand.*, **114**, 259.
WENDE, G. W. (1911): *J. Cutan. Dis.*, **29**, 1.
WESSELS, C. C. (1941): *Amer. Rev. Tub.*, **43**, 449, 459 and 637.
WILLIAMS, R. H., and NICKERSON, D. A. (1935): *Proc. Soc. Exp. Biol. and Med.*, **33**, 403.
ZIEGLER, E. (1875): "Experimentelle Untersuchungen über die Herkunft der Tuberkelelemente Staudinger." Würzburg.
ZIEGLER, E. (1906): "Lehrbuch der speziellen pathologischen Anatomie," 2nd Edit. Jena.

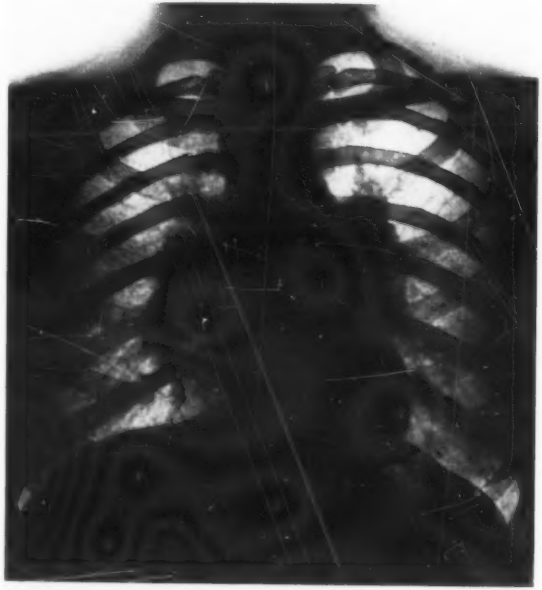

FIG. 1.

J. N. Female, aged 28. Recent bilateral iridocyclitis and hilar adenitis. Mantoux negative 1 : 100. Enlarged broncho-pulmonary lymph glands. Well two years later, when glands recessive.

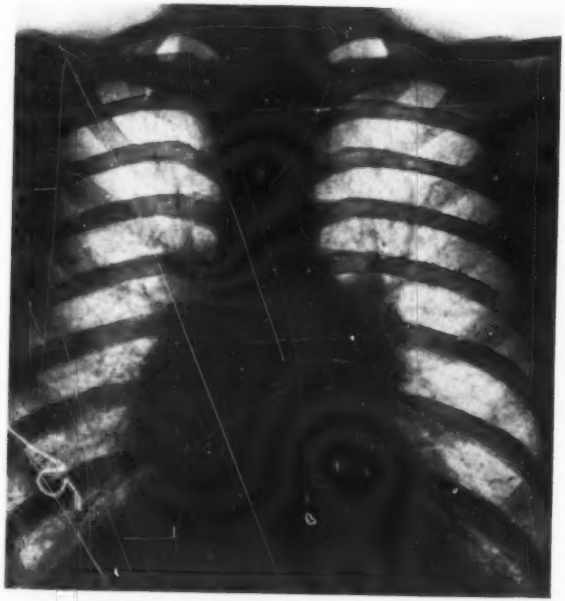

FIG. 2.

W. P. Male, aged 27. Splenomegaly and sarcoid lymphadenopathy. Biopsy control. Mantoux negative 1 : 100. Enlarged broncho-pulmonary lymph glands and reticulated lung fields. Recessive lesions two years later.

[To face p. 58

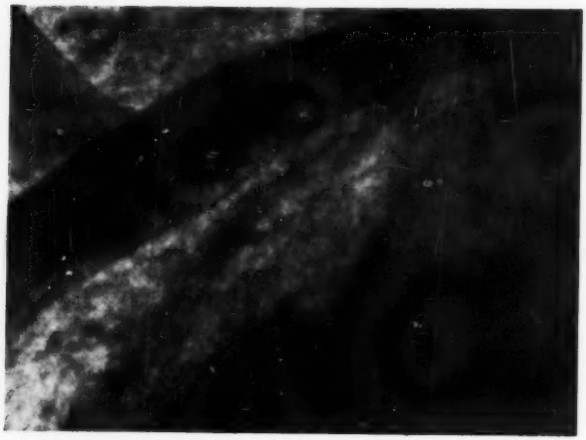

FIG. 2A.
Detail of right lung depicted in Fig. 2.

FIG. 3.
W. C. Female, aged 53. Ten years bilateral iridocyclitis and left facial palsy. "Asthma" five years. Mantoux negative 1 : 1,000. Enlarged broncho-pulmonary lymph glands and late reticulation in lung fields. No change three years later.

FIG. 4.

L. K. Female, aged 29. Seven years recurrent nodular cutaneous sarcoids, bilateral iridocyclitis and parotitis with right facial palsy. Progressive pulmonary fibrosing sarcoidosis with bilateral fibrocavernous tuberculosis eventually. Terminal cor pulmonale and right heart failure. Lymph gland biopsy and necropsy control. (See also Figs. 6, 11, 12, 13, 14 and 15.) Enlarged broncho-pulmonary lymph glands, late reticulation and some coarse nodulation in lung fields. Ten years before death.

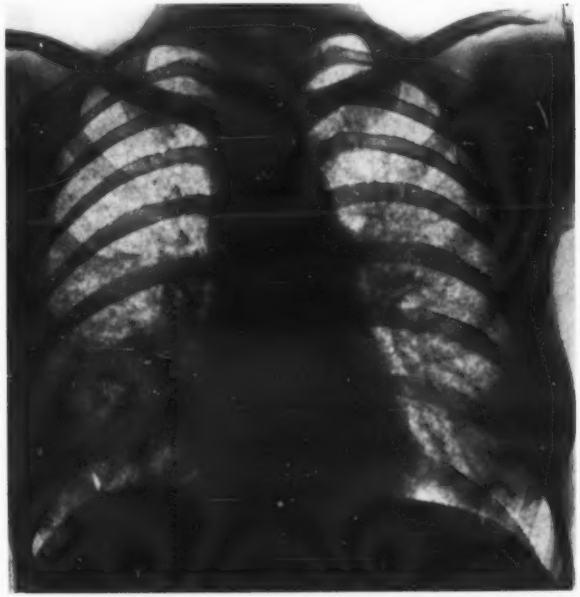

FIG. 5.

D. E. Female, aged 29. Eight years bilateral iridocyclitis, parotitis, polyneuritis and left facial palsy. Recurrent cutaneous sarcoids and splenomegaly. Biopsy control. Mantoux negative 1 : 100. Enlarged broncho-pulmonary lymph glands and miliary mottling throughout both lung fields. Alive and well ten years later, but with some diffuse residual pulmonary fibrosis and total blindness.

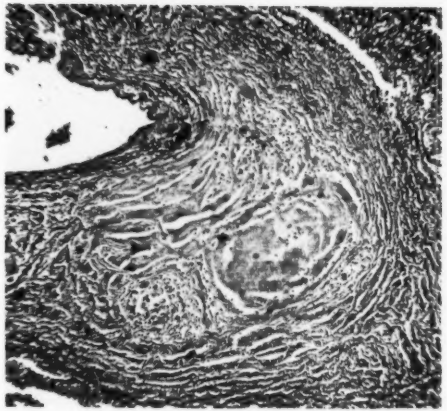

FIG. 6.

L. K. Female, aged 38. Section of lung. Left lower lobe. H and E. Two sarcoid foci, one completely hyalinised, in dense perivascular fibrous tissue. (See also Figs. 4, 11, 12, 13, 14 and 15.)

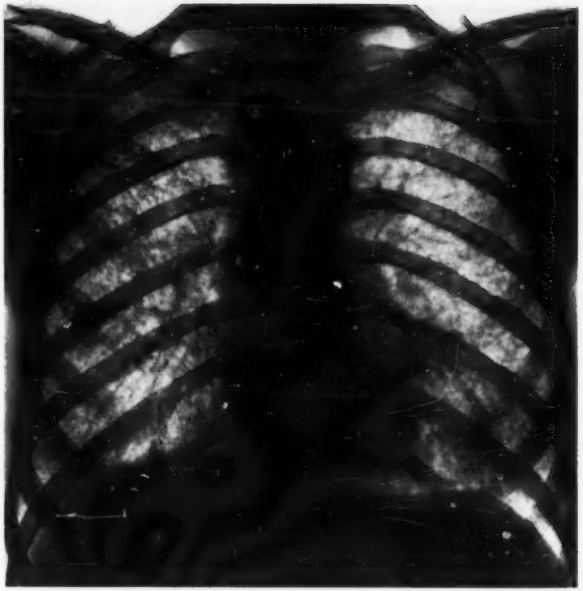

FIG. 7.

V. E. Female, aged 26. Chronic miliary tuberculosis. One year recurrent nodular cutaneous "sarcoid-like" lesions. Biopsy showed caseation and endarteritis. Mantoux negative 1 : 10. Alive and well nine years later, but with some residual pulmonary fibrosis.

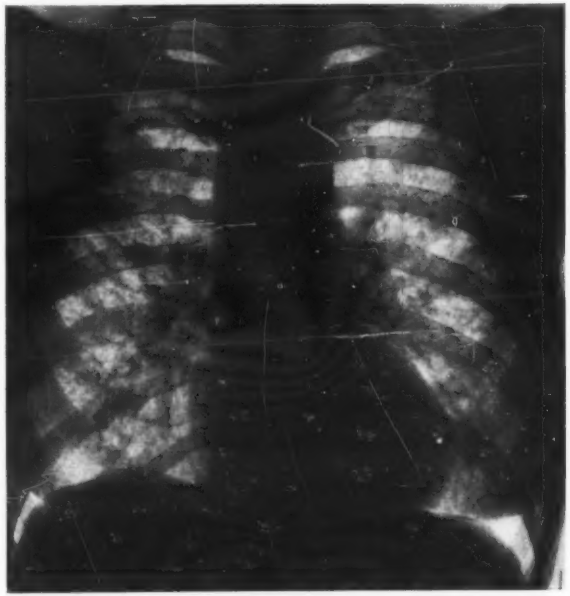

FIG. 8.

A. L. Female, aged 44. Splenomegaly, hilar adenitis and diffuse mottling both lungs. Mantoux positive 1 : 10,000.

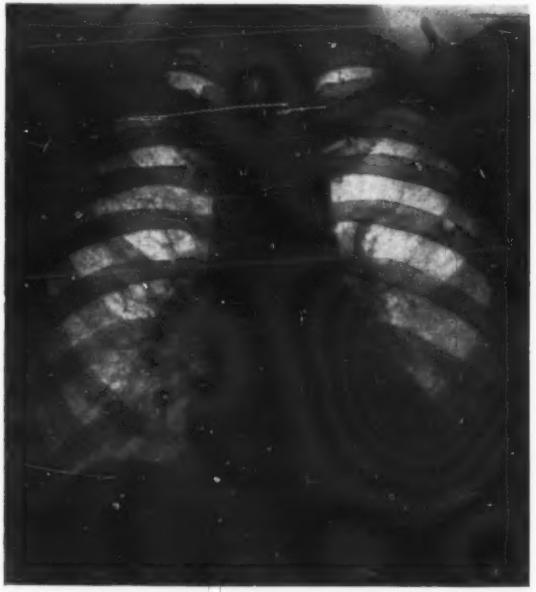

FIG. 9.

A. L. Female, aged 49. Five years later. Alive and well. Calcified hilar glands. Lung fields almost normal.

PLATE XIX.

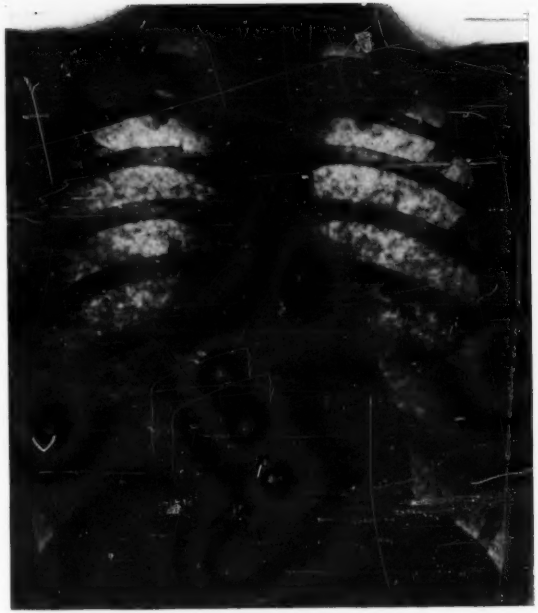

FIG. 10.

B. K. Female, aged 23. Chronic miliary tuberculosis. No proof for eighteen months, when tubercle bacilli in urine. Progressing renal and sacro-iliac tuberculosis subsequently. Died three years after this radiogram was taken. Necropsy control.

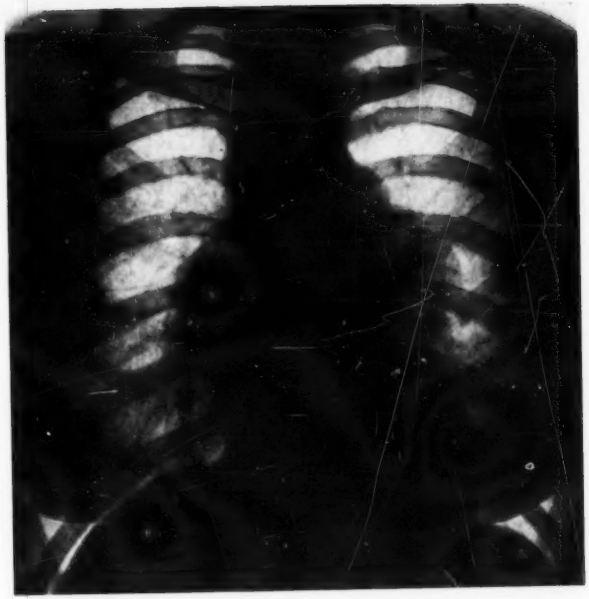

FIG. 11.

L. K. Female, aged 24. Recurrent nodular cutaneous sarcoids, bilateral iridocyclitis and parotitis with right facial palsy. Progressive pulmonary fibrosing sarcoidosis with bilateral fibrocavernous tuberculosis eventually. Terminal cor pulmonale and right heart failure. Necropsy control. Massively enlarged broncho-pulmonary lymph glands at onset. (See also Figs. 4, 6, 12, 13, 14 and 15.)

PLATE XX.

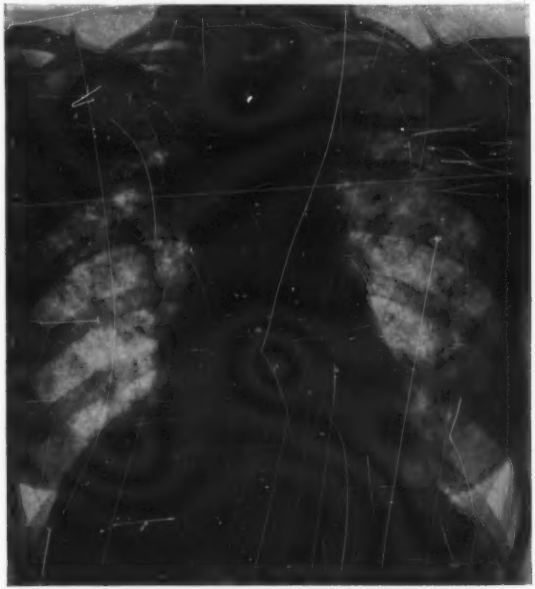

FIG. 12.

L. K. Female, aged 36. Twelve years later. Some glandular enlargement still present with fibrocaseous tuberculosis both upper lobes. Sputum T.B. present. Diffuse lymphogenous fibrosing sarcoidosis throughout rest of both lungs. Lymph gland biopsy and necropsy control. (See also Figs. 4, 6, 11, 13, 14 and 15.)

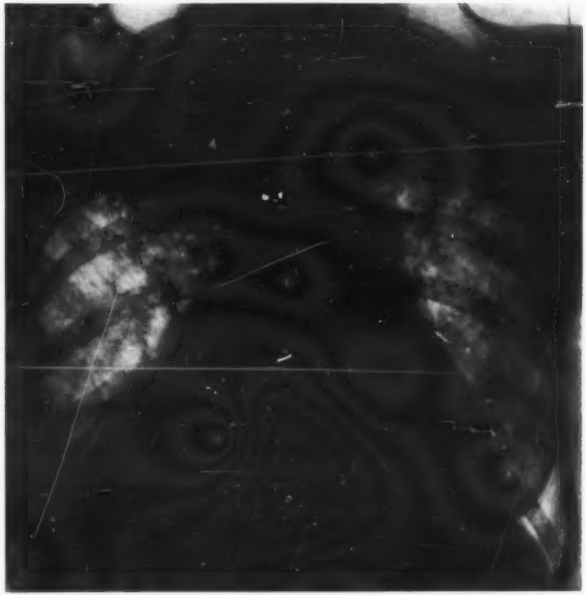

FIG. 13.

L. K. Female, aged 38. Two years later, shortly before death. Cavitated tuberculosis upper lobes. Diffuse lymphogenous fibrosing sarcoidosis rest of both lungs. Cor pulmonale with right heart failure. Lymph gland biopsy and necropsy control. (See also Figs. 4, 6, 11, 12, 14 and 15.)

FIG. 14.

L. K. Female, aged 38. Necropsy specimen of left lung. Extensive cavitated fibrocaseous tuberculosis upper lobe, and lymphogenous fibrosing sarcoidosis lower lobe. (See also Figs. 4, 6, 11, 12, 13 and 15.)

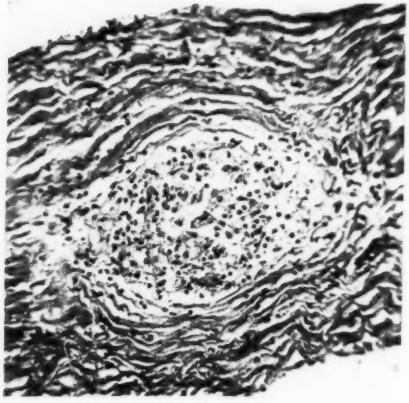

FIG. 15.

L. K. Female, aged 38. Section of lower lobe of left lung. H and E. Alveolar wall showing epithelioid sarcoid focus in dense hyalinising fibrous tissue. (See also Figs. 4, 6, 11, 12, 13 and 14.)

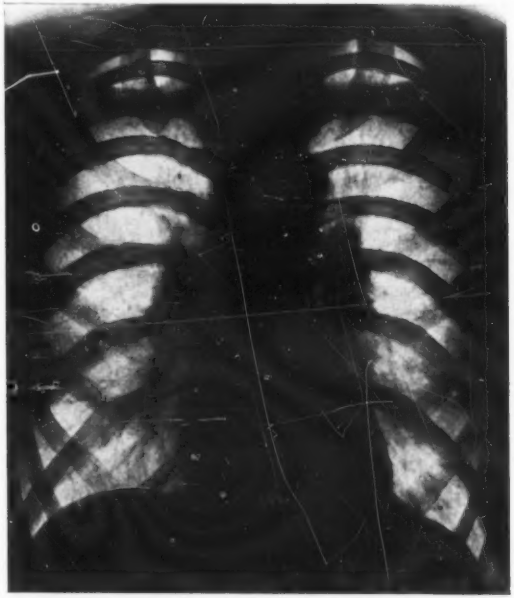

FIG. 16.

N. J. Male, aged 32. Recent sarcoid lymphadenopathy. Biopsy control. Calcified primary complex right lower zone. Mantoux positive 1 : 1,000. Enlarged broncho-pulmonary lymph glands and reticulated lung fields. Recessive lesions two years later.

FIG. 16A.

Detail of left lung depicted in Fig. 16. (See also Figs. 17 and 17A.)

PLATE XXIII.

FIG. 17.

N. J. Male, aged 34. Two years later. Symptomless and well. Broncho-pulmonary lymph glands nearly normal. Lung fields clear, except for calcified primary complex.

FIG. 17A.

Detail of left lung depicted in Fig. 17. (See also Figs. 16 and 16A.)

PLATE XXIV.

FIG. 18.

H. J. Female, aged 30. Recent hæmoptysis. Focal apical infiltrations, partly calcified, with primary complex right upper lobe included. (See also Figs. 19, 20 and 21.)

FIG. 19.

H. J. Female, aged 31. Fourteen months later. Apical infiltrations unchanged. Enlarged broncho-pulmonary lymph glands. Caseous tuberculous cervical adenitis (biopsy control). Mantoux negative 1 : 10. (See also Figs. 18, 20 and 21.)

To face p. 99]

FIG. 20.

H. J. Female, aged 34. Three years later. Focal calcifying apical infiltrations. Diffuse reticulation both lung fields and some small focal shadows. Enlarged broncho-pulmonary lymph glands now almost normal. Mantoux negative 1 : 10. Symptomless and well. (See also Figs. 18, 19 and 21.)

FIG. 21.

H. J. Female, aged 37. Three years later. Focal fibrous apical infiltrations with some calcification. Lung fields otherwise almost normal, though with broncho-vascular markings rather prominent. Broncho-pulmonary lymph glands normal. Mantoux negative 1 : 10. Symptomless and well. (See also Figs. 18, 19 and 20.)

NOTICE OF MEETING

JOINT TUBERCULOSIS COUNCIL

At the last meeting of the Joint Tuberculosis Council, congratulations were extended to Sir Robert Young, Dr. James Boyd, Dr. Norman Tattersall and Dr. G. S. Todd on their Birthday honours.

On the invitation of the Evidence Committee on Remuneration of Consultants and Specialists, the Council set down its views on the status and salaries of tuberculosis physicians in the National Health service. The Council considered that among the specialist officers employed by Regional Hospital Boards should be included a chief administrative and consultant tuberculosis officer, physicians in charge of clinical teams dealing with tuberculosis and their assistant physicians, the medical superintendents of sanatoria, and assistant physicians in sanatoria. Physicians in charge of the clinical teams should hold higher qualifications, and their status and remuneration should be identical with those of other consultants—*e.g.*, general physicians. Medical superintendents of sanatoria should also rank with general physicians and receive similar remuneration, with the addition of residential emoluments or their equivalent. Assistant tuberculosis physicians should correspond in status and remuneration to assistant general physicians.

The Joint Tuberculosis Council deputed Dr. D. P. Sutherland, Dr. James Watt and Dr. Norman England to attend, if invited, before the Spens Committee to give oral evidence in support of these views.

The Council adopted a resolution asking the Minister of Health to reconsider as a matter of urgency the fuel allowance for the families of tuberculous persons, in view of the steep rise in fuel prices since the original scale was fixed.

NOTICE

TUBERCULOSIS CARE COMMITTEES UNDER THE NEW NATIONAL HEALTH ACT, 1946

Tuberculosis Care Committees affiliated to the NAPT may be glad of a statement as to their legal position under the new National Health Service Act when it comes into force in 1948.

(1) Voluntary bodies not running actual medical services may continue as in the past.

(2) Where a Tuberculosis Care Committee runs a service, the local health authority may approve this service and continue it. A local health authority may, subject to the approval of the Minister of Health, contribute to a voluntary organization whose purpose is the prevention of illness, care and after-care, but may not pay money direct to patients.

(3) Local health authorities must submit any proposals for " the prevention of illness, care and after-care " to the Minister before August 31, 1947, and publish in the local press the date on which they do so. A copy of the proposals will be served on all voluntary organizations, including Tuberculosis Care Committees, which will have two months in which to make representations and objections, if any, to the Minister. Mr.

Bevan has asked that, where possible, prior consultations between local health authorities and such bodies should be held to devise an agreed scheme, and so save time by avoiding requests for subsequent modification.

The Secretary-General of the NAPT will be glad to advise any Care Committee on this matter.